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**RESEARCH ARTICLES**

# Correlation of Brain Derived Neurotrophic Factors (BDNF) With Maternal and Perinatal Outcome in Preeclampsia

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***Abstract***

***Objective****: To analyze the correlation between BDNF and maternal and perinatal outcomes in preeclampsia.*

***Methods****: This was an observational analytic study with cross-sectional design on 73 pregnant women with preeclampsia. The study began in January-June 2020 in Obstetrics and Gynecology Department of Dr M. Djamil Central General Hospital Padang.*

***Results****: The mean BDNF levels of pregnant women with preeclampsia were 519.9±325.4 pg/ml. The correlation between BDNF and systolic and diastolic blood pressure, and Mean Arterial Pressure was negatively correlated (r=-0.145, -0.1, and -0.218), with weak correlation and no statistically significant relationship between BDNF and systolic and diastolic blood pressure, and Mean Arterial Pressure (p>0.05). The correlation between BDNF and infant birth weight and length was positively correlated (0.196 and 0.205) with weak correlation, and between BDNF and APGAR score was negatively correlated (-0.039 and -0.054) with weak correlation, with no statistically significant correlation between BDNF with birth weight and length, and APGAR score (p>0.05).*

***Conclusion****: The mean BDNF level in preeclampsia was lower than normal pregnancy, there were negative correlation between BDNF and maternal outcomes with weak correlation, positive correlation between BDNF and perinatal outcomes and negative correlation between BDNF and APGAR score with weak correlation in preeclampsia.*

***Keywords:*** *Brain Derived Neurotrophic Factors, Preeclampsia, Maternal Outcome, Perinatal Outcome*

## INTRODUCTION

BDNF neurotrophin is highly expressed in blastocysts.[1,2] Activation of TrkB by BDNF stimulates the expression of Vascular Endothelial Growth Factor (VEGF) through Hypoxia Inducible Factor-1α (HIF-1α).[3,4] Increased expression of HIF-1α causes an increase in VEGF expression. VEGF is one of the angiogenesis factors that play an important role in regulating the development of the placenta.[2,5] BDNF neurotrophin also plays an important role in the regulation of angiogenesis and is reported to protect endothelial progenitor cells by increasing superoxide dismutase (SOD) expression. SOD is a metalloenzyme that catalyzes the dismutation of superoxide anions which is an important part of cellular antioxidants as a



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defence mechanism.[6]

The placentation process requires high angiogenesis factors to meet fetal oxygen and nutritional needs. Proangiogenic and anti-angiogenic factors work together in the development of the placenta. In preeclampsia, angiogenesis is ineffective because the cytotrophoblast fails to change the cell surface and adhesion molecules.[7] Abnormal alteration of the cytotrophoblast is the early detection that will cause placental ischemia. The impaired trophoblast invasion in preeclampsia causes intermittent arterial blood flow which creates a hypoxic environment leading to oxidative stress. Oxidative stress and inflammation are known to be closely related and play a major role in the pathogenesis of preeclampsia.[8,9]

Oxidative stress has been shown to affect the expression of neurotrophins, which are known to influence angiogenesis.[7] Increased oxidative stress can lead to the downregulation of neurotrophins.[10] Increased oxidative stress in pregnant women with preeclampsia causes BDNF levels to be lower when compared to normotensive pregnant women.[11,12]

Adaptation of the placenta to ensure optimal fetal growth during pregnancy is supported by an analysis of pathological findings in the placenta and factors circulating in the maternal circulation which in turn influence maternal and perinatal outcomes. Thus, based on these findings, we intended to conduct a study to see whether there was a correlation between BDNF levels in preeclampsia and maternal outcomes (SBP (Systolic Blood Pressure), DBP (Diastolic Blood Pressure) and MAP (Mean Arterial Pressure), and perinatal outcomes (body weight, body length, and APGAR score)

## METHOD

This was an analytic observational study with cross-sectional design. The research was conducted from January to September 2020 at Dr. M. Djamil Central General Hospital Padang in the Obstetrics and Gynecology Department with a total sample of 73 subjects. BDNF level examination was carried out at the Biomedical Laboratory of Faculty of Medicine, Andalas University.

The study sample was all pregnant women diagnosed with preeclampsia who fulfilled the inclusion and exclusin criteria. Inclusion criteria were mothers with a diagnosis of preeclampsia and were willing to be research respondents and had signed an informed consent form. Exclusion criteria were mothers with superimposed preeclampsia, damaged serem and drop-out patient during the study.

All samples had taken anamnesis, physical examination, laboratory examination and ultrasound examination and then blood samples were taken for BDNF examination according to procedure of Dr. M. Djamil Central General Hospital Padang. The blood samples were centrifuged in Clinical Pathology Laboratory of Dr. M. Djamil Central General Hospital Padang,



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and then the serum of the samples were delivered to Biomedical Laboratory Faculty of Medicine, Andalas University for BDNF levels examination using ELISA method.

Data processing used univariate analysis to determine the frequency distribution of each research variable, such as BDNF levels, maternal age, gestational age, parity, systolic blood pressure and diastolic blood pressure, MAP, BMI before pregnancy, infant weight, infant length and APGAR score. The next step was bivariate analysis to see the relationship between dependent variable, systolic blood pressure and diastolic blood pressure, MAP, BMI before pregnancy, infant weight, infant length and APGAR score with the independent variable, BDNF. Normality test was performed using the Kolmogorov Smirnov test (n < 100). If the data is normally distributed, the Pearson Correlation test is used, while if it is not normal, Spearman's Rank Correlation test is used.

## RESULTS

Characteristics of study subjects based on maternal age, gestational age, BMI, parity, BDNF, maternal outcomes (systolic blood pressure, diastolic blood pressure, MAP), and perinatal outcomes (body weight, body length, and APGAR score) shown in Table 1 below:

**Table 1.** Subject Characteristics and Research Variables

| Subject Characteristics | Mean ± SD | % |
|---|---|---|
| Maternal age (years) | 31.9 ± 6.7 | - |
| Gestational age (weeks) | 33.5 ± 4.2 | - |
| BMI (kg/m$^2$) | 28.1 ± 5.9 | - |
| Parity | | |
| Primipara | 21 | 28,8 |
| Multipara | 52 | 71,2 |
| BDNF (pg/ml) | 519.9 ± 325.4 | - |
| Systolic blood pressure (mmHg) | 171.4 ± 19.9 | - |
| Dyastolic blood pressure (mmHg) | 103.7 ± 12.7 | - |
| Mean Arterial Pressure (mmHg) | 141.8 ± 130.2 | - |
| Birth weight (grams) | 1930.9 ± 909.8 | - |
| Birth length (cm) | 42.1 ± 5.9 | - |
| 1$^{st}$ minute APGAR score | 4.7 ± 2.4 | - |
| 5$^{th}$ minute APGAR score | 6.4 ± 2.6 | - |

Based on table 1, it is known that the mean and frequency distribution of maternal characteristics for the maternal age are in the healthy reproductive age, whereas based on the characteristics of mean blood pressure and gestational age in this study, the subjects were



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most fell into severe preeclampsia with an early-onset (mean gestational age of 33.5 ± 4.2 weeks), the mean body mass index of the subjects was on the overweight group, and more than half of subjects with preeclampsia were multiparous. The mean BDNF levels in preeclampsia were lower than normal pregnancy, i.e. 4913 (2548-9551) pg/ml in the study by Luiza et al (2017).

**Correlation of BDNF Levels and Maternal Outcomes in Preeclampsia**

To determine the correlation between BDNF levels and maternal outcomes in preeclampsia, it can be seen in the following Scatter Plot chart**:**

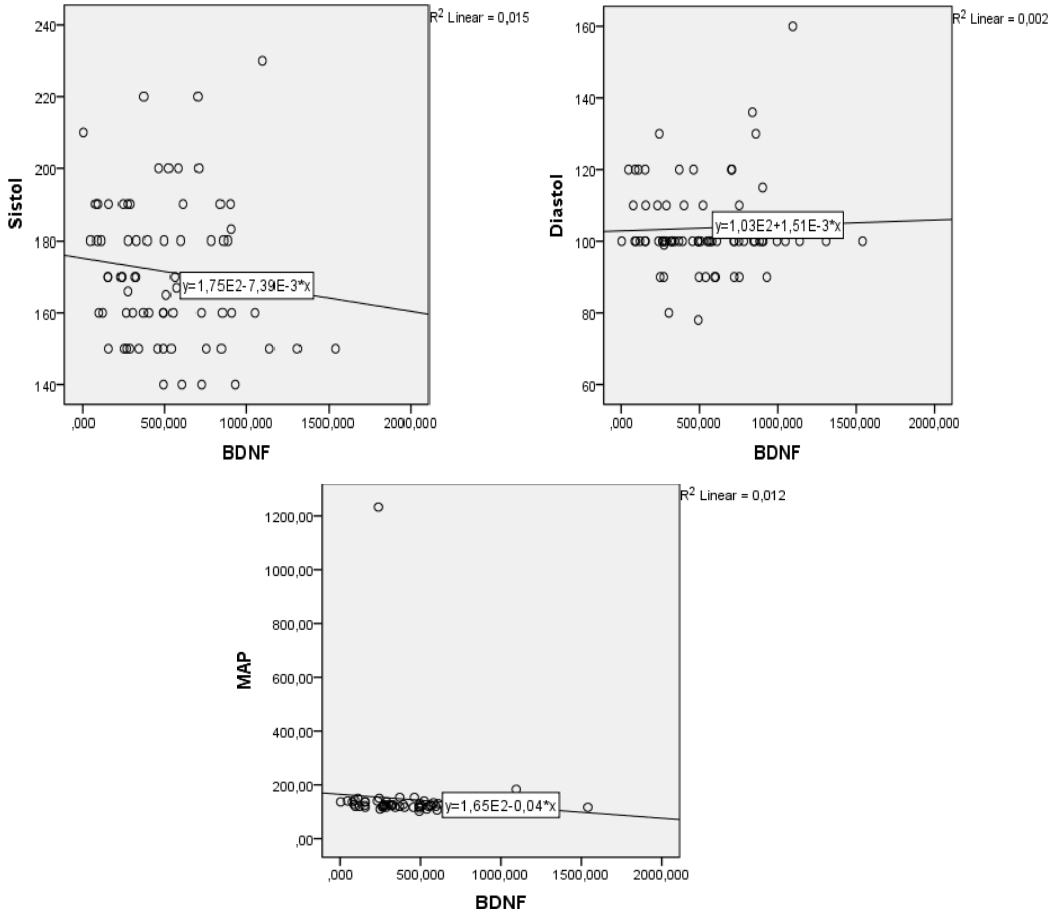


**Figure 1.** Correlation of BDNF levels with maternal outcomes.

Based on the Scatter Plot chart above (Figure 1), it can be concluded that the correlation between BDNF levels and maternal outcomes (systolic, diastolic, and MAP blood pressure) are negatively correlated, which means that the higher BDNF levels, the lower the systolic blood pressure. The R square values obtained were 0.015; 0.002, and 0.012 respectively, which means that BDNF levels affect systolic, diastolic, and MAP blood pressure of 1.5%, 0.2%, and



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1.2% respectively.

**Correlation of BDNF Levels and Perinatal Outcomes in Preeclampsia**

To determine the correlation between BDNF levels and perinatal outcomes in preeclampsia, it can be seen in the following Scatter Plot chart:

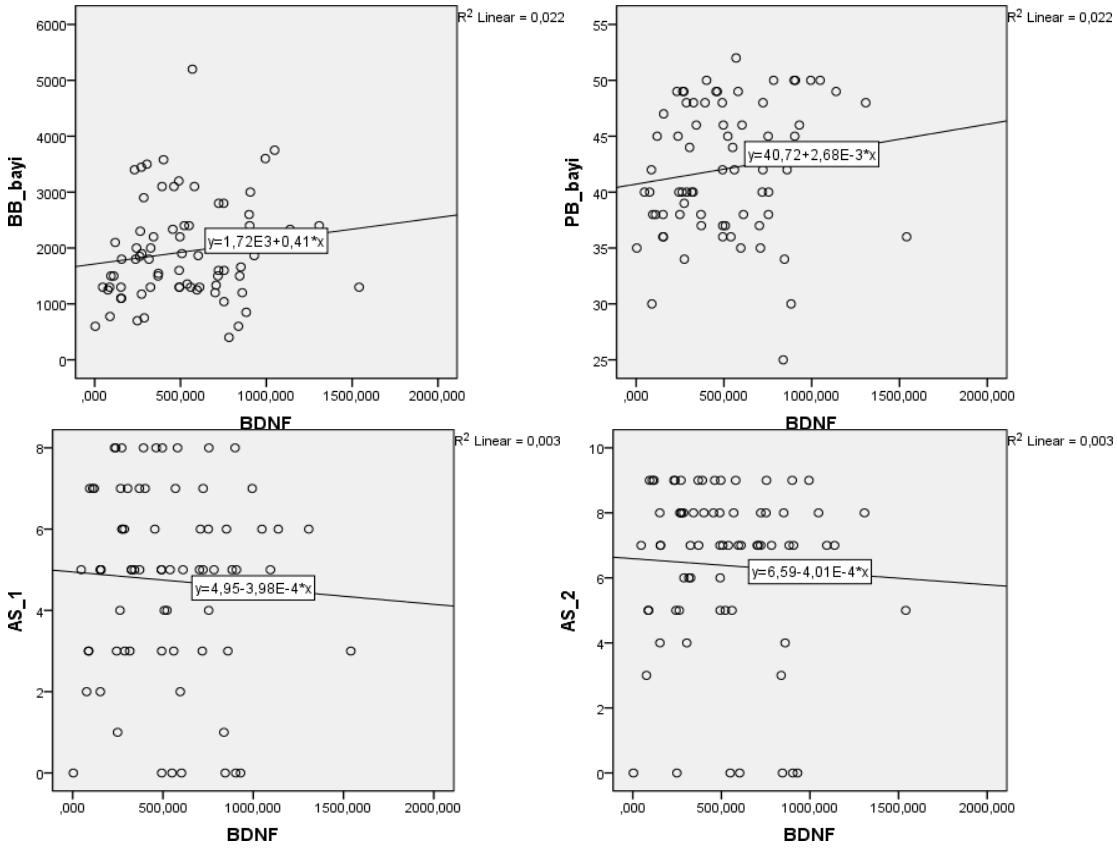


**Figure 2.** Correlation of BDNF levels with perinatal outcomes.

Based on the Scatter Plot chart above (figure 2), it can be concluded that the correlation of BDNF levels with the perinatal outcome (birth weight and birth length of newborns) is positively correlated. Both R square values were obtained 0.022, which means that BDNF levels affected the baby's birth weight and the baby's birth length, 2.2% respectively. Meanwhile, the correlation between BDNF levels and the APGAR score in the first and fifth minutes had a negative correlation. The R square value was 0.003, which means that BDNF levels affect the APGAR score for the first five minutes by 0.3%.

## DISCUSSION

From this study, it is known that the maternal age characteristics was in healthy reproductive age (31.9 ± 6.7 years). The mean gestational age was 33.5 ± 4.2 weeks,



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meanwhile from systolic and diastolic blood pressure, it was found that subjects were in severe preeclampsia (171.4 ± 19.9 and 103.7 ± 12.7 mmHg) with early-onset. More than half of the subjects were multiparous (71.2%) with the mean BMI before pregnancy was in overweight group (28.1 ± 5.9 kg/m$^2$).

The results of the mean age in this study differ from the other literature, where the high risk of preeclampsia, most often occurs in primigravidas with the age of <20 years or> 35 years.[1] The prevalence of severe preeclampsia that occurs in the healthy age range is due to the fact that pregnancy and childbirth mostly occur at the productive age of 20-35 years. This is not in line with the theoretical presentation, where the risk factors that increase the probability and severity of preeclampsia are mothers with the age of > 35 years, primiparity, previous maternal history or family history, and body mass index of> 30 kg/m$^2$. The multiparity factor is possible due to the aging process which makes physiological adaptation of pregnancy more difficult, increased comorbidity, and the occurrence of degenerative diseases or endothelial vascular damage. Additional factors such as previous pregnancy history and pregnancyinterval can increase the risk of developing preeclampsia in multiparity.[13]

The incidence of preeclampsia, in primiparous, is two times higher than that of multiparous women. This is thought to be due to the development of tolerance to specific immunological factors after the first pregnancy, thereby reducing the risk in subsequent pregnancies. These immunological factors are probably related to placental adaptation, in which the interactions between maternal and paternal immunological factors are most active. However, some experts believe that preeclampsia is driven by systemic circulation from the placenta, thus allowing paternal factors to influence systemic response.[14]

Adipose tissue is a strong supplier of inflammatory mediators, making obese women more likely to increase an excessive inflammatory response, thus a BMI of > 35 kg/m$^2$ is associated with an increased risk of preeclampsia. Sohlberg et al (2012) in their study found that BMI appeared to be stronger in relation to late-onset preeclampsia or mild preeclampsia, whilst early-onset preeclampsia and severe preeclampsia originated from abnormal placentation, while late-onset preeclampsia and mild preeclampsia were more often associated with metabolic disease and more often associated with a higher BMI. A high BMI causes an increase in blood pressure through the secretion of angiotensinogen by adipocytes, an increase in blood viscosity due to the secretion of pro fibrinogen and plasminogen activator inhibitor (PAI) by adipocytes, and an increase in blood volume due to increased body mass.[15]

**Mean BDNF Level with Preeclampsia**

The results of this study indicate that the mean BDNF level of pregnant women with preeclampsia was 519.9 ± 325.4 pg/ml. This study was in line with the study by Dhobale et al (2012) which explained that the mean BDNF level in preeclampsia was 505.26 ± 174.97



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pg/ml.[11] Not much different from the study by D'Souza et al (2014), where it was known that the mean BDNF level on the third- trimester preeclampsia was 426 ± 118 pg / mL and 462 ± 151 pg / mL in the second trimester.[3]

Perucci et al (2017) explained that plasma BDNF concentrations in women with preeclampsia were lower than women with normal pregnancies, but there was no significant difference in BDNF levels between late-onset and early-onset preeclamptic patients.[1]

The low levels of BDNF are influenced by the increase in oxidative stress. The imbalance of pro-angiogenic factors and anti-angiogenic factors is caused by low levels of BDNF, which causes endothelial disorders, dysfunction, and damage, causing clinical manifestations of preeclampsia.[3,4]

The decrease in BDNF will cause downregulation of MMP-9 which plays a role in trophoblast invasion and the growth and development of trophoblasts and placenta thereby increasing cell apoptosis.[16] BDNF neurotrophin is also known to play an important role in the regulation of angiogenesis and reportedly protects endothelial progenitor cells by increasing superoxide expression dismutase (SOD).[17] This imbalance of proangiogenic and anti-angiogenic factors will lead to clinical manifestations of preeclampsia. Thus, it can be hypothesized that activation of the BDNF / TrkB system in fetomaternal conditions under oxidative stress can lead to the incidence of preeclampsia.[4]

**Correlation of BDNF Levels and Maternal Outcomes in Preeclampsia**

Based on the results of this study, it is known that the correlation between BDNF and systolic blood pressure, diastolic blood pressure, and mean arterial pressure was negatively correlated (r = -0.145, -0.1, and -0.218), which means that the lower the BDNF level, the higher the systolic blood pressure, diastolic blood pressure, and mean arterial pressure, with a weak correlation. The results of the analysis showed that there were no significant differences between BDNF and systolic blood pressure, diastolic blood pressure, and mean arterial pressure (p> 0.05).

In line with the study by D'Souza et al (2014) which explained that maternal BDNF levels were negatively related to systolic blood pressure (r = - 0.176, p = 0.034, df = 143) and diastolic blood pressure (r = - 0.261, p = 0.002, df = 143).[1] In contrast to the results of a study conducted by Luiza et al (2017), it showed that BDNF levels were positively correlated with diastolic blood pressure (r = 0.334, p = 0.046), meaning that preeclamptic women with higher BDNF concentrations have higher diastolic blood pressure, and the mean diastolic blood pressure in preeclampsia was 102 mmHg, while a normal pregnancy was 70 mmHg.[12] Currently there are no studies linking BDNF levels to MAP in preeclampsia.

The differences in the correlation in this study may be due to differences in blood pressure concentrations between the studied populations. Circulating BDNF concentration



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can be affected by several factors such as lifestyle-related to health, such as cigarette use, alcohol, diet, and nutrition. Genetic factors, race, demographics, stressors, inflammation, and hormonal factors.[18,19]

Lee et al (2018) stated that low BDNF serum levels were associated with vascular resistance. In one cross-sectional study, low BDNF levels were associated with central nervous system disorders and arterial stiffness. Arterial stiffness describes the loss of elastic capacity of the artery walls to withstand blood flow fromventricular ejection. Widened pulse pressure, due to a spike in systolic pressure in the undisturbed artery wall followed by low diastolic pressure, reflects the severity of arterial stiffness. Arterial stiffness causes not only extracellular damage to the vessel walls but also dysfunction of vascular smooth muscle cells. The TrKB receptor has a high affinity for BDNF and is expressed in vascular smooth muscle. Thus, the inactivation of the BDNF-TrkB signaling pathway in vascular smooth muscle cells can interfere with the integrity and function of blood vessels.[20]

Endothelial dysfunction, which occurs due to a decrease in BDNF levels, causes an imbalance in the production of substances that act as vasoconstrictors such as endothelium I, thromboxane, and angiotensin II which cause extensive constriction of blood vessels, stimulating hypoxia in the uteroplacental circulation. Low BDNF levels will lead to poor maternal outcomes such as increased blood pressure and target organ disorders.[21]

**Correlation of BDNF Levels and Perinatal Outcomes in Preeclampsia**

Based on the results of this study, it is known that the correlation between BDNF and birth weight and the birth length were 0.196 and 0.205 respectively, which means that the lower the BDNF level, the lower the birth weight and birth length,with a weak correlation. The correlation between BDNF levels and the APGAR score at the first minute and the fifth minute was negatively correlated (-0.039 and -0.054).

Weight and length of infants in this study led to preterm biometry, in line with the mean gestational age in this study. APGAR scores at the first and fifth minutes in this study showed moderate hypoxia occurred in newborns. Currently, there are no studies that link BDNF levels with the APGAR score. In this study, there was no significant relationship between BDNF levels with birth weight, birth length, and APGAR score.

D'Souza et al (2014) explained that there were no significant differences in fetal characteristics (birth weight, birth length, head circumference, and chest circumference) in women with preeclampsia and normal pregnancy (p> 0.05). Another study, conducted by Puchner et al (2007) also stated that there was no statistically significant difference in BDNF levels between IUGR infants and term babies.[22]

In contrast to the research conducted by Ardiani et al (2019) in which they compared the mean BDNF levels between normal infants and IUGR, it is known that there were



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statistically differences in the mean BDNF levels between the two groups. The mean BDNF level in normal infants was higher, i.e. 1.58 ± 0.23 ng / mL while it was 1.25 ± 0.35 ng / mL in infants with IUGR.[23] A study by Christian et al (2016) showed that serum BDNF level was significantly lower in the 3rd trimester (p = 0.004) in women who delivered low birth weight babies (<2500 g). For every 100 pg/ml reduction in serum BDNF level in the 3rd trimester, it was associated with a 3.5 times higher risk for the birth of a baby with low birth weight.[19]

This study did not classify the mode of delivery in the subject. A study by Flock et al (2016) showed that the results of differences in the mode of delivery and time of delivery also affect circulating maternal and neonatal BDNF levels. The mean maternal BDNF and fetal cord serum levels were higher in vaginal delivery than cesarean surgery.[24]

This study also did not differentiate the gestational age and prenatal administration of corticosteroids that could affect the perinatal outcome. Based on a study conducted by Nitin et al (2003), it was shown that in normal pregnancy, cord BDNF levels increase with gestational age. Cord BDNF levels in preterm fetuses who did not receive prenatal corticosteroids were lower than in fetuses receiving prenatal corticosteroids.[25]

The influence of maternal nutrition on the epigenetic program is very important in the prenatal and early postnatal development period and when the epigenetic mechanism is maturing. Changes in micronutrient levels in a one-carbon cycle can induce oxidative stress, either by affecting folic acid levels or interfering with homocysteine remethylation. Changes in the metabolism of micronutrients such as folic acid, vitamin B12, and DHA through one-carbon cycle can regulate neurotrophic factors epigenetically. Changes in the one-carbon cycle can also affect the epigenetic program of the placenta.[26]

Factors that affect fetal growth, including maternal nutrition, are intrauterine environmental factors that affect the development of the fetoplacental unit. In this study, there was no data collection on maternal nutrition during early pregnancy. Adequate maternal nutrition plays an important role in protecting the embryo from deficiencies, which can occur early in pregnancy when the placenta is not yet formed.[27]

Other factors that influence fetal weight are changes in the supply of nutrients to the fetus, genetic and environmental factors, the hormonal and nutritional supply of the placenta which depends on size, morphology, blood flow, and placental transfer. In women who have a lower weight of the placenta, it can lead to an insufficient flow of the placenta to the fetus.[10,11,27]

The source of neurotrophin BDNF for the growth and development of the placenta and fetus is also obtained from the mother. BDNF has been shown to penetrate across the placental barrier. The increase in BDNF is shown on umbilical cord blood examination with increasing gestational age. The placenta is a temporary central organ uniquely designed to carry nutrients, gases, antibodies, hormones, growth factors, and waste products between mother



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and fetus. The study in recent years has shown that neurotrophins play an important role in the regulation of placental development and fetal growth.[28]

BDNF neurotrophin has been shown to regulate placental development in maternal-fetal relationships and act both paracrine and endocrine. BDNF and growth factors are proteins that are involved in angiogenesis and aid in placental development. It is explained that the lack of intake of certain nutrients during pregnancy affects gestational duration, placental growth, and fetal growth during pregnancy. It is known that changes in the metabolism of micronutrients such as folic acid, vitamin B1, long- chain polyunsaturated fatty acids (LCPUFA), and docosahexaenoic acid (DHA) through a one-carbon cycle can regulate neurotrophic factors epigenetically, which play an important role in normal fetal placental development and maturation of the brain and central nervous system functions.[26]

APGAR Score is closely related to changes in acid-base balance and provides an overview of the severity of cardiovascular changes which is used to determine whether the baby has asphyxia or not at birth. APGAR score is influenced by maternal and fetal factors. Fetal factors such as prematurity, hypoxia, acidosis, twisted umbilical cord, cord obstruction, presentation abnormalities such as breech presentation, and others. While maternal factors are pregnancy (infection, preeclampsia/eclampsia, diabetes, heart disease) and the delivery process (cesarean section, vacuum extraction, forceps extraction).[29] In our study, we did not differentiate between the length of time of delivery and the mode of delivery, thus it is necessary to carry out further research on the relationship between BDNF levels and the mode of delivery and the length oftime of delivery.

## CONCLUSION

From the results of this study, it can be concluded that the mean BDNF levels in preeclampsia were lower than in normal pregnancy. There was a negative correlation between BDNF levels and maternal outcomes (systolic blood pressure, diastolic blood pressure, and mean arterial pressure) in preeclampsia with a weak correlation. There was a positive correlation between BDNF levels and perinatal outcomes (body weight and baby length) in preeclampsia and there was a negative correlation between BDNF levels and APGAR score in preeclampsia with a weak correlation.

## REFERENCES

1. Vandita A. D'Souza , Anitha S. Kilari , Asmita A. Joshi , Savita S. Mehendale, Hemlata M. Pisal, and Sadhana R. Joshi. Differential Regulation of Brain Derived Neurotrophic Factor in Term and Preterm Preeklampsia. Reproductive Sciences 2014. 21(2). DOI: 10.1177/1933719113493512 rs.sagepub.com
2. Fujita, K. Tatsumi, K. Kondoh, E. Chigusa, Y. Mogami, H. Fujii, T. et al. (2011).



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Differential expression and the antiapoptotic effect of human placental neurotropins and their receptors. Placenta . Fung, J. Gelaye, B.Qiu-Yue Z. Rondon, MB

3. Vandita D'Souzaa, Vidya Patila, Hemlata Pisala, Karuna Randhira, Asmita Joshia,Savita Mehendaleb, Girija Waghb, Sanjay Guptec, Sadhana Joshia, 2014. Levels of brain derived neurotrophic factors across gestation inwomen with preeklampsia. Int. J. Devl Neuroscience 37. Hal 36–40. ELSEVIER
4. M. Dhobale. Neurotrophic : Role in Adverse Pregnancy Outcome. International Journal Of Developmental Neuroscience Volume 37. Elsevier, 2014:8– 14.
5. Darwin Muhammad , Handono Kalim, Djoko Wahono S, Aru W Sudoyo, Fatchiyah. Hypoxia-Inducible Factor-1α Expression Induce Erythropoietin and Vascular Endothelial Growth Factor Expression on Breast Cancer with Anemia. Jurnal Kedokteran Brawijaya 2012. Vol. 27, No. 2.
6. Nakamura, K. Martin, KC. Jackson, JK. Beppu, K. Chan-Wook,W. & Thiele, CJ. (2006). Brain-Derived Neurotrophic Factor Activation of TrkB Induces Vascular Endothelial Growth Factor Expression via Hypoxia-Inducible Factor-1A in Neuroblastoma Cells. American Association for Cancer Research
7. Frisca, Caroline T. Sardjono,Ferry Sandra. Angiogenesis: Patofisiologi dan Aplikasi Klinis. JKM. Vol.8 No.2 Februari 2009: 174-187
8. Lungguk Helen Alfian Tanjung, Sri Sulistyowati, Supriyadi Hari R, 2017. The Effect Of Vascular Endothelial Growth Factor 121 Recombinant Against Expression Of Heat Shock Protein 70 In Mice (Mus Musculus) Model Preeklampsia. Https://Eprints.Uns.Ac.Id/32348/1/S501208018_. Pdf
9. Sahay, AS. Sundrani, DP. & Joshi, SR, 2017. Neurotropins: Role in Plasental Growth and Development. In G. Litwack, Neurotropins. USA: Elsevier. pp. 243-260.
10. Gardiner, J., Barton, D., Overall, R., Marc, J., 2009. Neurotrophic support and oxidative stress: converging effects in the normal and diseased nervous system. Neuro- scientist 15, 47–61.
11. Dhobale M, Mehendale S, Pisal H, D'Souza V, Joshi S. Association of brain- derived neurotrophic factor and tyrosine kinase B receptor in pregnancy. Neuroscience. 2012;216:31-37
12. Luiza Oliveira Perucci, Érica Leandro Marciano Vieira, Antônio Lúcio Teixeira, Karina Braga Gomes, Luci Maria Dusse, Lirlândia Pires Sousa. Decreased plasma concentrations of brain-derived neurotrophic factor in preeklampsia. L.O. Perucci et al. / Clinica Chimica Acta 464, 2017.142–147
13. Husen, D &Polin, A. 2012. Factors Influencing Maternal Mortality from Severe Preeclampsia and Eclampsia.MajObstetGinekolog Indonesia 2012; 36-2: 90-4
14. Duckitt K, Harrington D. Risk factors for pre-eclampsia at antenatal booking:



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systematic review of controlled studies. BMJ. 2005 Mar 12;330(7491):565

15. Sohlberg S, Stephansson O, Cnattingius S, et al. 2012. Maternal body mass index, height, and risks of preeklampsia. Am J Hypertens 25(1): 120-125.
16. Kazuhiro Kawamura, Nanami Kawamura, Wataru Sato, Jun Fukuda, Jin Kumagai,and Toshinobu Tanaka.,Brain-Derived Neurotrophic Factor Promotes Implantation and Subsequent Placental Developmentby Stimulating Trophoblast Cell Growth and Survival. Endocrinology 2009.150(8):3774–3782
17. Rosemary Kraemer, Barbara L. Hempstead. Neurotropin : Mediator Terbaru Angiogenesis. Frontiers in Bioscience 2003 (8): s1181-1186
18. M. Dhobale. Neurotrophic Factors and Maternal Nutrition During Pregnanc. BioTRaK Research and Diagnostics Centre, Navi Mumbai, India.Elsevier, 2017. Volume 104, ISSN 0083-6729
19. Lisa M. Christian, Amanda M. Mitchell, Shannon L. Gillespie, and Marilly Palettas. Serum brain-derived neurotrophic factor (BDNF) across pregnancy and postpartum: Associations with race, depressive symptoms, and low birth weight. Psychoneuroendocrinology. 2016 December ; 74: 69–76. doi:10.1016/j.psyneuen.2016.08.025.
20. I-Te Lee, Wayne Huey-Herng Sheu, Wen-Jane Lee , Der-Yuan Chen. Serum brain-derived neurotrophic factor predicting reduction in pulse pressure after a one-hour rest in nurses working night shifts. *Scientific Reports* volume 8, https://doi.org/10.1038/s41598-018-23791-8
21. Helmo, Fernanda Rodrigues. Et.al. Angiogenic and antiangiogenic factors in preeklampsia. Pathology - Research and Practice. Elsevier. 2018
22. Puchner AM, Nikolaou KE, Economou E, Boutsikou M, Boutsikou T, Kyriakakou. M. Intrauterine growth restriction and circulating neurotrophin levels at term. Early Human Development 2007;83:465-9.
23. Ardiani Y, Defrin, Husna Yetti, 2019. Kajian Pustaka: Kadar Brain Derived Neurotrophic Factor Mempengaruhi Berat Badan Lahir pada Bayi. Jurnal Ilmiah Universitas Batanghari Jambi Volume 19, Nomor 1, Februari; Hal 152-155
24. Flöcka, S.K. Weber a, N. Ferrari b, C. Fietz b, C. Graf b, R. Fimmers c, U. Gembrucha, W.M. Merz. Determinants of brain-derived neurotrophic factor (BDNF) in umbilical cord and maternal serum A. Psychoneuroendocrinology 63 (2016) 191–19.
25. Nitin S. Chouthai, Jackie Sampers, Nirmala Desai, And George M. Smith. Changes In Neurotrophin Levels In Umbilical Cord Blood From Infants With Different Gestational Ages And Clinical Conditions. Pediatric Research 2003 ;Vol. 53, No. 6. Doi: 10.1203/01.Pdr.0000061588.39652.26
26. M. Dhobale. Neurotrophic Factors and Maternal Nutrition During Pregnanc. BioTRaK



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*http://jurnalobgin.fk.unand.ac.id/index.php/JOE*

Research and Diagnostics Centre, Navi Mumbai, India.Elsevier, 2017. Volume 104, ISSN 0083-6729

27. S. Mayeur, M. Silhol, Moitrot, S. Barbaux , Breton, A. Gabory ,Vaiman, I. Dutriez-Casteloot, I. Fajardy, A.Vambergue,Tapia-Arancibia, B. Basti, Stormea,B, C. Junien F, D. Vieau A,B, J. Lesage A, 2010. Placental Bdnf/Trkb Signaling System Is Modulated By Fetal Growth Disturbancesin Rat And Human. Placenta 31. Doi 785e791. Elsevier.
28. Sahay A.S, D.P. Sundrani, G.N. Wagh, S.S. Mehendale , S.R. Joshi. Neurotropin levels in different regions of the placenta and their association with birth outcome and blood pressure. 2015. http://dx.doi.org/10.1016/j.placenta.2015.06.006. Elsevier.
29. Rudolph, M., Hoffman, E.J., Rudolph, D.C., 2006. Buku Ajar Pediatrik. Edisi 20. EGC. Jakarta.



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